IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

TAKEDA PHARMACEUTICALS U.S.A., INC., Plaintiff, v. WEST-WARD PHARMACEUTICAL CORPORATION, HIKMA AMERICAS INC., and HIKMA PHARMACEUTICALS PLC, Defendants.	Civil Action No. 14-cv-1268-SLR

PLAINTIFF TAKEDA PHARMACEUTICALS U.S.A., INC.'S BRIEF IN SUPPORT OF ITS MOTION PURSUANT TO FEDERAL RULES OF CIVIL PROCEDURE 59(E) AND 15(A) FOR A MODIFICATION OF THE JUDGMENT OF DISMISSAL AND FOR LEAVE TO AMEND ITS COMPLAINT

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Date: June 3, 2016

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Plaintiff Takeda Pharmaceuticals U.S.A., Inc. ("Takeda") respectfully submits this brief in support of its motion brought pursuant to Federal Rules of Civil Procedure 59(e) and 15(a) for a modification of the judgment of dismissal entered on May 18, 2016, to permit Takeda to file the Proposed Second Amended Complaint, attached to the Motion as Exhibit A.[1]

I. NATURE AND STAGE OF THE PROCEEDINGS

On October 3, 2014, Takeda filed suit against West-Ward Pharmaceutical Corporation, Hikma Americas Inc., and Hikma Pharmaceuticals PLC (collectively, "Hikma") asserting induced infringement of five of Takeda's patents under 35 U.S.C. § 271(b). *See* D.I. 1. On October 9, 2014, the Court issued a temporary restraining order ("TRO"). D.I. 21, D.I. 54. On November 4, 2014, the Court denied Takeda's request for a preliminary injunction ("PI") but provided for the maintenance of the TRO pending appeal. D.I. 78. On appeal, the Federal Circuit affirmed the court's denial of a PI and vacated the TRO. *Takeda Pharms. U.S.A, Inc. v. West-Ward Pharm. Corp.*, 785 F.3d 625, 627 (Fed. Cir. 2015). On September 10, 2015, Takeda filed its First Amended Complaint. D.I. 109. On October 1, 2015, Hikma moved to dismiss under Federal Rule of Civil Procedure 12(b)(6). D.I. 112. On May 18, 2016, the Court granted Hikma's motion to dismiss and the Clerk of the Court closed the case. D.I. 121, D.I. 122.

II. SUMMARY OF THE ARGUMENT

1. After the entry of an order dismissing its complaint pursuant to Federal Rule of Civil Procedure 12(b)(6), a plaintiff may properly request that the court alter or amend its judgment to permit amendment of the complaint. Under Third Circuit law (which governs procedural issues),

[1] Pursuant to District of Delaware Local Rule 15.1, Takeda's Proposed Second Amended Complaint ("PSAC") is attached as Exhibit A to Takeda's motion. A redline copy of the Proposed Second Amended Complaint showing the changes from the First Amended Complaint (D.I. 109) filed on September 10, 2015, is attached as Exhibit B to Takeda's motion.

such requests are governed by the Rule 15(a) standards regarding leave to amend the pleadings: this Court should "freely give leave when justice so requires." Fed. R. Civ. P. 15(a)(2).

2. The most important factor in determining whether to grant leave to amend is whether the amended pleading states a proper claim. Takeda has amended its allegations to clearly state a claim based on Hikma's active encouragement of third-party infringement, **including Mitigare sales representatives' statements telling healthcare providers to prescribe Mitigare for the unapproved indications covered by Takeda's patents, including for the treatment of acute gout flares, and its distribution of a sales aid which explicitly references the ACR Guidelines that recommend Takeda's patented methods.** Takeda has also alleged that these actions have achieved their intended purpose of inducing infringement and has specified how Takeda's patents are directly infringed.

3. The other Rule 15(a) factors also favor Takeda's request for amendment.

- Takeda's request for leave to file an amended complaint is timely.
- Takeda submits the proposed amendment in good faith to correct what the Court held to be deficiencies in its allegations regarding Hikma's infringement. Takeda has both (i) clarified its earlier allegations and (ii) added new information learned since the First Amended Complaint was filed.
- The present motion does not reflect repeated failures to cure defects in the complaint. Takeda's original complaint was based on Hikma's *prospective* infringement before Hikma began selling its colchicine products. The First Amended Complaint was Takeda's first opportunity to present allegations of *past* infringement based on Hikma's actual Mitigare sales, and the current amendment is only the second complaint directed to such infringing acts. Further, as discussed below, Takeda's proposed complaint includes additional information uncovered after the filing of the First Amended Complaint.
- As discovery has not begun, Hikma will not suffer prejudice from the amendment.

III. STATEMENT OF FACTS

On September 26, 2014, Hikma obtained FDA approval to market Mitigare (colchicine) 0.6 mg capsules for the prophylaxis of gout flares. Takeda learned of the FDA's action from a

Hikma press release dated September 30, 2014, and filed its original Complaint, D.I. 1, on October 3, 2014. That same day, Hikma launched its Mitigare product and, shortly thereafter, prepared to launch a Mitigare authorized generic ("Mitigare AG").

In the original Complaint, Takeda alleged that the FDA-approved Mitigare label would induce infringement of five patents relating to the use of colchicine to treat and prevent gout flares. Two of the patents recite methods for administering colchicine in low doses to treat acute gout flares (collectively, the "Acute Gout Flare Patents"). The other three patents recite methods for administering colchicine in reduced doses to prevent gout flares in patients concomitantly taking specific drugs which are "CYP3A4" or "P-gp" inhibitors (collectively, the "Drug-Drug Interaction" or "DDI Patents"). Because Mitigare was not yet being sold when Takeda filed its original Complaint, Takeda sought an injunction against such sales.

Since January 9, 2015, when the Federal Circuit affirmed this Court's denial of a preliminary injunction and vacated its TRO pending appeal, Hikma has been selling and offering for sale both Mitigare and the authorized generic version of Mitigare (collectively, the "Mitigare Products" or "Mitigare"). Hikma agreed to allow Takeda to file an amended complaint that addressed its sales and marketing activities. D.I. 108, D.I. 109. On September 10, 2015, Takeda filed a First Amended Complaint including allegations regarding the steps Hikma had taken in its sales and marketing activities, ***outside*** of the instructions in its label, to encourage actual infringement of the patented methods.[2] Hikma again moved to dismiss. D.I. 112, D.I. 113.

On May 18, 2016, the Court issued a memorandum opinion and order granting Hikma's motion to dismiss. D.I. 121. With respect to the Acute Gout Flare Patents, the Court held that

[2] The First Amended Complaint also added allegations of induced infringement directed to an additional Acute Gout Flare Patent, the '395 patent, as well as two additional DDI Patents, the '297 patent and the '004 patent. *See* D.I. 109.

Takeda had not sufficiently pled induced infringement. After reasserting its PI ruling that the statements in Hikma's product label did not induce infringement, the Court turned to the new allegations relating to Hikma's post-launch marketing and sales activities. The Court held that such allegations were "too conclusory to pass muster," and did not adequately allege "active steps" taken by Hikma to "encourage direct infringement." *Id.* at 17.

With respect to the DDI Patents, the Court stated that, "based on the record currently before it, the court maintains its finding [in its PI Order] that Takeda has not adequately alleged direct (and consequently, induced) infringement." *Id.* at 18-19. The Court held that Takeda's complaint alleged only "speculative future infringement," concluding that "[i]t is undisputedly *possible* that the use of Mitigare™ will not ever practice the claimed method." *Id.* (emphasis added). The Court also held that the DDI Patents cannot be practiced with Hikma's product, stating that "[d]irect infringement of the DDI Patents requires a 0.3 mg dose of colchicine per day; Mitigare™ is a 0.6 mg capsule that cannot be split." *Id.* at 18. The Court did not separately reach the question of Takeda's inducement allegations concerning the DDI Patents.

IV. LEGAL STANDARDS

After the entry of final judgment, Federal Rule of Civil Procedure 59(e) provides a plaintiff with a "window in which to seek to reopen the judgment and amend the complaint." *Fletcher-Harlee Corp. v. Pote Concrete Contractors, Inc.*, 482 F.3d 247, 253 (3d. Cir. 2007).[3] Under Rule 59(e) "[a] motion to alter or amend a judgment must be filed no later than 28 days after the entry of the judgment."[4]

[3] Internal citations and quotations omitted unless otherwise noted.

[4] The filing of a motion under Rule 59 also tolls the period for filing a notice of appeal. *See* Fed. R. App. P. 4(a)(4)(A)(iv); *Fletcher-Harlee Corp.*, 482 F.3d at 253 n.8 ("Rule 59 motions have the added benefit of tolling the 30-day window for filing a notice of appeal.").

The Third Circuit has made clear that "[u]nder [its] precedent, leave to amend within this window should, as Federal Rule of Civil Procedure 15(a) puts it, 'be freely given when justice so requires.'" *Fletcher-Harlee Corp.*, 482 F.3d at 253 (quoting Fed. R. Civ. P. 15(a)). When a plaintiff files a Rule 59(e) motion accompanied by a Rule 15(a) motion after the dismissal of a complaint under Rule 12(b)(6), "the appropriate manner to dispose of this issue is to consider the motions together and determine what outcome is permitted by consideration of the Rule 15(a) factors." *Burtch v. Milberg Factors, Inc.*, 662 F.3d 212, 231 (3d Cir. 2011); *see also Holland v. Simon Prop. Grp., Inc.*, 495 F. App'x 270, 273 (3d Cir. 2012) ("Where [] the Rule 59(e) motion is timely filed, the District Court should consider the factors set forth in Federal Rule of Civil Procedure 15(a) when determining whether to grant the postjudgment motion to amend.").

"Under Rule 15(a), if a plaintiff requests leave to amend a complaint vulnerable to dismissal before a responsive pleading is filed, such leave must be granted in the absence of undue delay, bad faith, dilatory motive, unfair prejudice, or futility of amendment." *Grayson v. Mayview State Hosp.*, 293 F.3d 103, 108 (3d Cir. 2002); *Foman v. Davis*, 371 U.S. 178, 182 (1962) ("In the absence of any apparent or declared reason—such as undue delay, bad faith or dilatory motive on the part of the movant, repeated failure to cure deficiencies by amendments previously allowed, undue prejudice to the opposing party by virtue of allowance of the amendment, futility of amendment, etc.—the leave sought should, as the rules require, be freely given.").

While all of the factors recited above are relevant to whether to allow leave to amend, the most important factor is whether the proposed amendment cures the deficiencies the Court has identified in the complaint. "[I]f a claim is vulnerable to dismissal under Rule 12(b)(6), but the plaintiff moves to amend, leave to amend generally must be granted unless the amendment

would not cure the deficiency." *Shane v. Fauver*, 213 F.3d 113, 115 (3d Cir. 2000); *see, e.g.*, *Linkerhof v. Delaware Soc'y for the Prevention of Cruelty to Animals*, No. CA 11-256-LPS, 2012 WL 769603, at *5 (D. Del. Mar. 9, 2012) (granting Plaintiff leave to amend as "the facts suggest that Plaintiff may be able to state a claim" and citing *Phillips v. Cty. of Allegheny*, 515 F.3d 224, 236 (3d Cir. 2008) ("[I]f a complaint is vulnerable to 12(b)(6) dismissal, a district court must permit a curative amendment, unless an amendment would be inequitable or futile.")).

V. ARGUMENT

The Proposed Second Amended Complaint is timely presented and is made in good faith for the purpose of remedying the defects that this Court concluded were present in the First Amended Complaint. Accordingly, there has been no delay, bad faith, or repeated failures to cure. As this case has not advanced to discovery, there also is no prejudice to Hikma. Finally, the proposed amendment cures the deficiencies identified by the Court in its decision. Thus, and as set forth in detail below, leave to amend is warranted.

A. Takeda's Proposed Amendment is Timely

Takeda has not delayed in seeking leave to amend. Takeda brings this motion approximately two weeks after the Court entered an order dismissing the First Amended Complaint and in advance of the deadline for such motions. *See* D.I. 121; Fed. R. Civ. P. 59(e) (motions must be brought within 28 days of entry of judgment or order).

B. The Proposed Second Amended Complaint is Offered for a Proper Purpose

While Takeda respectfully believes that the allegations in its First Amended Complaint sufficed to state a proper claim, it has further amended its complaint to address what the Court perceived to be deficiencies in its factual allegations. Amending a complaint to rectify pleading defects identified by the court is entirely proper. *See, e.g., Pennsylvania Emp., Benefit Trust Fund v. Zeneca, Inc.*, 710 F. Supp. 2d 458, 487 (D. Del. 2010) (amendment permitted to "cure

the deficiencies with the Amended Complaint") (Robinson, J.); *Endo Pharm. Inc. v. Mylan Techs. Inc.*, No. CIV.A. 11-220-GMS, 2013 WL 936452, at * 3(D. Del. Mar. 11, 2013) (same).

Moreover, the unusual procedural posture in which the Court decided Hikma's motion to dismiss presents particularly compelling reasons why Takeda may properly seek amendment. When Takeda filed its First Amended Complaint, the pleading requirements governing direct patent infringement were set forth in Form 18 of the Federal Rules of Civil Procedure. *See* D.I. 115 at 8. Form 18 required only that a complaint contain "(1) an allegation of jurisdiction; (2) a statement that the plaintiff owns the patent; (3) a statement that defendant has been infringing the patent by making, selling, and using [the device] embodying the patent; (4) a statement that the plaintiff has given the defendant notice of its infringement; and (5) a demand for an injunction and damages." *In re Bill of Lading Transmission & Processing Sys. Patent Litig.*, 681 F.3d 1323, 1334 (Fed. Cir. 2012); *see, e. g.*, *Select Retrieval, LLC v. Bulbs.com Inc.*, No. CIV.A. 12-10389-TSH, 2012 WL 6045942, at *4 (D. Mass. Dec. 4, 2012) ("barebones" allegations are "all that Form 18 requires".). The First Amended Complaint met this standard. *See* D.I. 109 ¶¶ 10-18 (jurisdictional allegations); ¶¶ 2, 28 (Takeda owns the asserted patents); ¶¶ 68, 77, 81, 85, 93 (statements that others are directly infringing the claims of the DDI Patents using Mitigare); Prayer for Relief (requesting injunction and damages); *see* D.I. 1, 109 (providing notice).

On September 10, 2015, when Takeda filed its First Amended Complaint, Form 18 was still in effect. Form 18 remained in effect on November 16, 2015, the date on which the motion was fully submitted and ripe for decision. Thus, had the Court decided the motion in November, the Form 18 standard would have governed Takeda's direct infringement allegations.

As it turned out, the Court did not decide Hikma's motion prior to the December 1, 2015 abrogation date for Form 18. During oral argument on March 29, 2016, Takeda argued that the

sufficiency of its direct infringement allegations should be evaluated against the Form 18 standard that was in effect both when the First Amended Complaint was filed and when the motion was fully briefed, citing precedent.[5] Ex. 1 to Br. (Hearing Tr. at 35:3-36:8). In its decision, however, the Court applied the *Twombly/Iqbal* plausibility standard in evaluating Takeda's allegations of direct infringement. *See* D.I. 121 at 7-8 (citing *Ashcroft v. Iqbal*, 556 U.S. 662 (2009) and *Bell Atl. Corp. v. Twombly*, 550 U.S. 544 (2007) and not mentioning Form 18); *id*. at 19 ("Given the lack of factual allegations of infringement, the court is unable to find that Takeda has a 'plausible claim for relief' at this time. *Iqbal*, 556 U.S. at 679.").

Takeda continues to maintain that the *Twombly/Iqbal* standard should not govern allegations of direct infringement in a complaint, and related motion to dismiss, filed before the abrogation of Form 18. Indeed, Takeda respectfully submits that it is unfair for the standard for assessing the sufficiency of its direct infringement allegations to have depended on whether the Court decided the present motion before or after December 1, 2015. Takeda accepts, however, that the Court elected to apply the new standard. What is relevant for purposes of the present motion, is that the intervening change in the pleading requirements provides a compelling reason to allow amendment of the complaint. *See, e.g.*, *Fulk v. Vill. of Sandoval*, No. CIV. 08-843-GPM, 2009 WL 1606897, at *2 (S.D. Ill. June 9, 2009) (granting leave to amend "[b]ecause of the recent change in federal pleading standards"); *Coal. For A Level Playing Field, L.L.C. v. AutoZone, Inc.*, 737 F. Supp. 2d 194, 219 (S.D.N.Y. 2010) (permitting plaintiff to propose curative amendments where "the Court [] dismiss[ed] a complaint filed prior to a change in the pleading standards on the basis of those new standards"); *Boarhead Farm Agreement v.*

[5] *See Hologram USA, Inc. v. Pulse Evolution Corp.*, No. 2:14-CV-0772-GMN NJK, 2016 WL 199417, at *2 n.1 (D. Nev. Jan. 15, 2016); *Lubrizol Specialty Prods., Inc. v. Flowchem LLC*, No. CV H-15-2917, 2016 WL 775033, at *1-2 (S.D. Tex. Feb. 29, 2016).

Advanced Envtl. Tech. Corp., 381 F. Supp. 2d 427, 431 (E.D. Pa. 2005) ("One of the circumstances under which courts have granted a motion for leave to amend a complaint is an intervening change in applicable law."). Here, Takeda respectfully submits that it should be permitted to allege direct infringement of the DDI Patents under the *Twombly/Iqbal* standards.

C. Takeda Has Not Repeatedly Failed to Cure Previously Identified Deficiencies in Its Complaint

Takeda is not guilty of "repeated failures to cure" perceived defects in its allegations. This is Takeda's second attempt to amend its complaint. The purpose of the first amendment was to convert a Hatch-Waxman declaratory relief action seeking to enjoin the launch of Hikma's product into a more traditional patent infringement suit based upon acts of infringement occurring after the Mitigare launch. The Court's dismissal order was thus the first decision addressing the sufficiency of Takeda's allegations with regard to Hikma's actual sales activities. Under these circumstances, Rule 15(a) counsels in favor of allowing Takeda an opportunity to amend its complaint to address the defects identified by the Court.

D. Hikma Will Not Be Prejudiced Should Amendment Be Permitted

Allowing amendment will not cause Hikma any cognizable prejudice. Discovery in this action has not begun, and thus Hikma will have a full and fair opportunity to direct its discovery to the allegations in the amended complaint. Moreover, Takeda is not seeking to introduce new claims or causes of action, but merely to supplement the factual allegations underlying the induced infringement claims present in its First Amended Complaint. *See, e.g.*, *Endo Pharm. Inc.*, 2013 WL 936452, at *3 (no prejudice where Defendant had notice of infringement claim and "the amendment does not substantially change the underlying theory of the case").

While allowing amendment would keep the case active and defer a final resolution, these are the inevitable consequences of allowing any amendment to a previously dismissed complaint,

and do not constitute the type of prejudice that justifies denial of leave to amend. *See, e.g.*, *Adams v. Gould Inc.*, 739 F.2d 858, 869 (3d Cir. 1984) (rejecting argument that "delay[ing] the end of the case" constitutes prejudice).

E. Amendment Is Not Futile

Finally, leave to amend should be granted because Takeda's proposed amendments are not futile. "'Futility' means that the complaint, as amended, would fail to state a claim upon which relief could be granted." *Shane*, 213 F.3d at 115. "In assessing 'futility,' the District Court applies the same standard of legal sufficiency as applies under Rule 12(b)(6)." *Id.* As detailed below, Takeda's Proposed Second Amended Complaint properly states a claim for infringement of both the Acute Gout Flare Patents and the DDI Patents.

1. The Proposed Second Amended Complaint States a Claim for Induced Infringement of the Acute Gout Flare Patents

The Court dismissed Takeda's Acute Gout Flare Patent infringement allegations because it concluded that Takeda had not adequately alleged inducing acts by Hikma. Specifically, the Court found that Takeda failed to allege sufficient "active steps" taken by Hikma to "encourage direct infringement." D.I. 121 at 17-18. The Proposed Second Amended Complaint adds new allegations of active steps taken by Hikma to encourage direct infringement and augments Takeda's previous allegations.

(a) The Proposed Second Amended Complaint alleges that Hikma has taken active steps to promote third-party infringement.

In its First Amended Complaint, Takeda alleged that Hikma engaged in post-marketing activities that induced infringement of the Acute Gout Flare Patents:

> (i) Mitigare sales representatives told providers that a 30-capsule supply of Mitigare—which is a sufficient supply for acute gout flare treatment but not for prophylaxis—could last a patient a full year; and

(ii) Hikma entered into "sole-source contracts" with healthcare providers, such as Kaiser Permanente, by which it supplies colchicine for all indications, including the treatment of acute gout flares.

The Court held that these allegations failed to rise to the level of active steps to encourage infringement. In response to the Court's ruling, in its Proposed Second Amended Complaint, Takeda has both (i) added new allegations of inducing conduct based on facts learned since the filing of the First Amended Complaint and (ii) augmented its factual allegations regarding Hikma's post-marketing activity to show how it supports a "plausible" claim of inducement.

(b) Hikma's liability for inducement is not limited to the statements in the Mitigare label.

As an initial matter, the Court in its opinion held that the sufficiency of Takeda's inducement claims was governed by analysis of Hikma's product label, as in cases such as Warner-Lambert Co. v. Apotex Corp., 316 F.3d 1348, 1364-65 (Fed. Cir. 2003). However, as the Federal Circuit itself emphasized in Warner-Lambert, the focus on the product label in evaluating an inducement claim is a characteristic of claims brought under 35 U.S.C. § 271(e)(2) of the Hatch-Waxman Act. Such claims are based on a generic applicant's filing of an ANDA seeking FDA approval to market the generic version of a brand drug protected by a patent. Such claims thus allege an "artificial act of infringement," because no actual infringement, in the form of sales of the generic drug, has yet occurred. Id. at 1358 (Hatch-Waxman Act "created an artificial act of infringement that consists of submitting an ANDA"). In such cases, the only "proof" of infringement is typically the product label submitted by the applicant to the FDA.

Here, in contrast, Takeda's claims are traditional infringement claims based on Hikma's infringing sales of Mitigare. Such claims are not subject to the same restrictions in proof as section 271(e)(2) claims. Id. at 1364-65 ("That a generic maker may someday induce someone to infringe can only be determined when that act occurs, and § 271(e)(2) was not designed to

cover such future acts.") (emphasis added). Instead, and as explained below, Takeda's current inducement claims properly are based on Hikma's marketing and sales activities.

(c) Takeda has added allegations that Mitigare salespeople have actively encouraged prescribers to infringe the Acute Gout Flare Patents by expressly telling them that Mitigare may be used to treat acute gout flares.

Takeda has added several new allegations based on information it has obtained since the filing of the First Amended Complaint. Specifically, new Paragraphs 52 and 53 allege that Hikma sales representatives have falsely represented to physicians that Mitigare: (i) is and does "the exact same thing" as Colcrys® and may be administered for Colcrys® for all indications for which Colcrys® is approved; (ii) is FDA-approved for acute gout flare treatment; and (iii) is substitutable for Colcrys® at the pharmacy level. New Paragraph 53 further alleges that Hikma sales representatives have explicitly urged prescribers to prescribe Mitigare for the acute indication. *Id.* ¶ 53. New Paragraph 54 further alleges that such salespeople: (i) are aware that Mitigare is not approved to treat gout flares; (ii) intend by their statements that healthcare providers prescribe Mitigare to treat acute flares; and (iii) know and intend, or are willfully blind to the fact that these providers will prescribe Mitigare according to the patented methods that represent the standard of care for acute gout flare treatment. *See id.* ¶ 54.

New Paragraph 65 adds further allegations regarding Hikma's recent contract with Express Scripts, a Pharmacy Benefit Manager. This contract specifies that all Colcrys® prescriptions handled by Express Scripts—including prescriptions for acute gout flare treatment—are to be filled with one of the Mitigare Products. Takeda alleges that, by entering into this contract, Hikma has actively encouraged Express Scripts to fill acute gout flare prescriptions with Mitigare in violation of Takeda's patent rights. *See id.* ¶ 65.

New paragraphs 57-61 add allegations regarding a promotional sales aid ("Mitigare sell sheet") that Hikma distributes to healthcare providers. This sell sheet specifically refers customers to the American College of Rheumatology ("ACR") Guidelines that recommend the use of the patented methods of the Acute Gout Flare Patents. *See id.* ¶¶ 57-61. These paragraphs further allege that, by expressly directing customers to the standards of care based on the patented methods, Hikma has actively encouraged prescribers to infringe Takeda's Acute Gout Flare Patents. *Id.* ¶ 61.[6]

(d) Takeda plausibly alleges that Hikma sales representatives' statements that a 30-capsule supply of Mitigare may last a patient a full year have actively encouraged third-party infringement of the Acute Gout Flare Patents.

As noted above, Takeda alleges that Hikma sales representatives have told their customers that a 30-capsule supply of Mitigare can last a patient a full year. In its Order, the Court held that "telling a patient that thirty capsules may last a year in no way constitutes '[e]vidence of active steps taken to encourage direct infringement.' *Takeda*, 785 F.3d 630 (alteration in original)." D.I. 121 at 17-18. Takeda has accordingly supplemented its factual allegations regarding this marketing activity to show how Hikma's conduct constitutes active steps to induce infringement.

New Paragraph 50-51 allege that: (i) thirty capsules is *not* a sufficient year-long supply for a patient taking Mitigare for prophylaxis, the only indication for which Hikma purportedly sells Mitigare; (ii) a thirty-capsule supply, on the other hand, can be an adequate year-long supply for treating acute gout flares; (iii) Hikma sales representatives who tell physicians that a

[6] This sell sheet, which cites to the ACR Guidelines, constitutes "labeling" under FDA law. *See* 21 C.F.R. § 202.1(l)(2); 21 U.S.C. § 321(m). Thus, even though Takeda's allegations are not limited to Hikma's labeling, this sell sheet forms a part of that labeling.

thirty-capsule supply can last a full year are aware of the foregoing facts; and (iv) such representatives, in telling these providers that a 30-capsule prescription is an adequate year-long supply, intend to encourage, and do encourage, these individuals to use Mitigare for acute gout flare treatment, a use for which it is not approved. PSAC ¶¶ 50-51.

Further, Takeda alleges that these representatives have encouraged healthcare providers to follow Takeda's patented dosing regimen when they use Mitigare to treat a gout flare. New Paragraph 54 alleges that Hikma salespeople are aware that there is only one method of colchicine acute gout flare treatment recommended by the ACR and approved by the FDA, namely, Takeda's patented low dose regimen. It further alleges that, in encouraging these healthcare providers to prescribe Mitigare for acute gout flare treatment, Hikma's salespeople specifically intend, or, alternatively, are willfully blind to the fact, that these providers will administer the drug according to Takeda's patented methods, and thus directly infringe Takeda's Acute Gout Flare Patents. *Id.* ¶ 54. Takeda further alleges that Hikma's inducing acts have resulted in third-party direct infringement. *Id.* ¶¶ 61, 66.

(e) Takeda has plausibly alleged that Hikma has actively encouraged infringement of the Acute Gout Flare Patents by healthcare providers with whom it has entered into its sole source contracts.

The Court held that Takeda's allegations regarding Hikma's solicitation of sole-source healthcare provider contracts, whereby Hikma agreed to supply healthcare organizations with Mitigare for all purposes, not merely for its FDA-approved indication for gout prophylaxis, "merely acknowledge[d] potential infringement by others, not that Hikma has taken 'active steps' itself to encourage direct infringement.'" D.I. 121 at 18.

Takeda has supplemented its allegations with regard to Hikma's conduct to highlight Hikma's active encouragement of its customers' infringement. New Paragraphs 62-64 allege that Hikma sales representatives: solicited sole-source negotiations with healthcare providers

knowing that those providers previously had purchased Colcrys® from Takeda; knew that these healthcare providers had been administering Colcrys® to patients both for prophylaxis and for acute gout flare treatment; knew that, in order to convince these healthcare providers to switch away from Takeda, Hikma needed to supply them with Mitigare for all uses for which they previously had prescribed Colcrys®, including for the treatment of acute gout flares; and discussed the providers' anticipated Mitigare requirements, including the fact that they would be purchasing Mitigare both for gout prophylaxis and to treat gout flares. PSAC ¶¶ 62-64. Here too, Takeda properly alleges that Hikma has intended to sell Mitigare for the unapproved use of treating acute gout flares.

New Paragraph 63 further alleges that Hikma representatives involved in negotiating these sole-source contracts, like the Hikma sales representatives discussed earlier, were aware that there is only one method of colchicine acute gout flare treatment recommended by the ACR and approved by the FDA, namely, Takeda's claimed low-dose regimen. *Id.* ¶ 63. Takeda further alleges that, in order to obtain these sole-source contracts, these Hikma representatives encouraged third parties to purchase Mitigare to treat acute gout flares intending, or, alternatively, being willfully blind to the fact that they prescribe the drug according to Takeda's patented methods, thus infringing Takeda's Acute Gout Flare Patents. *See id.* ¶ 64.

The Proposed Second Amended Complaint further alleges that Hikma's inducing acts have resulted in infringement. Takeda alleges that Kaiser Permanente's medication guide specifically instructs Kaiser physicians to administer Mitigare according to Takeda's patented low-dose regimen. *See id.* ¶ 66. The Proposed Second Amended Complaint further alleges that physicians have followed the medication guide with regard to prescribing Mitigare, and, in doing so, have administered Mitigare in a manner that infringes Takeda's patents. *Id.*

(f) Many of the facts demonstrating Hikma's inducement are within Hikma's and third parties' control.

Lastly, facts relating to the vast majority of interactions between Hikma and its customers and other third parties that underlie Takeda's inducement claims lie within the control of Hikma or these third parties. In its opinion, the Court faulted Takeda for failing, at the pleading stage, to cite more specific evidence of Hikma's inducing activities "despite having had at least ten months to observe the market's relation to Mitigare™." D.I. 121 at 17. However, absent discovery, Takeda has no way to obtain direct evidence of Hikma's communications with third parties, or to determine the extent to which third parties use Mitigare in infringing ways.

In recognition of this dilemma, Rule 11 of the Federal Rules of Civil Procedure permits a party to allege factual contentions that "will likely have evidentiary support *after* a reasonable opportunity for further investigation or discovery." Fed. R. Civ. P. 11(b)(3) (emphasis added). Courts interpreting the Rule have thus recognized that a party is permitted to "aver facts that they believe to be true, but that lack evidentiary support at the time of the pleading." 2 Moore's Federal Practice, § 8.04[4](Matthew Bender 3d Ed.).

Importantly, *Twombly/Iqbal* did *not* change this standard. *Arista Records LLC v. Doe 3*, 604 F.3d 110, 120 (2d Cir. 2010) (*Twombly* standard permits pleading on information and belief where facts are peculiarly within the possession and control of the defendant or when belief is based on information that makes inference of culpability possible); *accord Greene v. BMW of N. Am.*, Civ. No. 2:11-04220 (WJM), 2014 WL 47940, at *3 (D. N.J. Jan. 7, 2014) (*citing Arista)*. Nor do *Twombly* and *Iqbal* require a complainant to allege *evidence*, as opposed to facts, to support its claim. *See Whitney v. Guys, Inc.*, 700 F.3d 1118, 1128 (8th Cir. 2012) ("We refuse . . . to incorporate some general and formal level of evidentiary proof into the 'plausibility' requirement of *Iqbal* and *Twombly*"). As illustrated above, those facts which Takeda can

currently allege based on initial investigation more than suffice to establish a plausible claim against Hikma for induced infringement. In addition, however, Paragraphs 68 and 80 in Takeda's Proposed Second Amended Complaint specifically allege that many other facts demonstrating Hikma's encouragement and promotion of infringement likely are within the possession and control of Hikma and such third parties. *See* PSAC ¶¶ 68, 80. Takeda should be allowed to use the tools of discovery to obtain evidence of such facts.

(g) The Proposed Second Amended Complaint alleges a proper claim for inducement of the Acute Gout Flare Patents.

As the Supreme Court stated in *Iqbal*, "[w]hen there are well-pleaded factual allegations, a court should assume their veracity and then determine whether they plausibly give rise to an entitlement to relief." *Iqbal*, 556 U.S. at 679. Here, the new proposed amended complaint contains a host of allegations that Hikma's representatives have described Mitigare as a product that should be used to treat acute gout flares. There can be no clearer basis for an inducement claim than Hikma's active encouragement of its customers and prescribers to use Mitigare for an indication for which Mitigare not only is not approved, but for which the standard of care is a patented treatment method that neither Hikma nor its customers have a right to practice. The facts alleged go far beyond mere knowledge of third-party infringement, and cross over into active aiding and abetting such infringement. Such conduct states a claim for inducement.

2. The Proposed Second Amended Complaint States a Claim for Direct Infringement of the DDI Patents

Turning to the DDI Patents, the Court dismissed the First Amended Complaint because it concluded that Takeda had not properly alleged direct (and thus induced) infringement of the DDI Patents. D.I. 121 at 18. In applying *Twombly/Iqbal*'s plausibility standard, the Court found several deficiencies with Takeda's allegations. The Proposed Second Amended Complaint remedies the alleged deficiencies found by the Court and thus is not futile.

(a) The Proposed Second Amended Complaint pleads direct infringement of the DDI Patents.

The Court held that Takeda's allegations with regard to the DDI Patents "are insufficient to raise a reasonable inference of infringement." D.I. 121 at 19. Specifically, the Court stated that "[i]t is undisputedly possible that the use of Mitigare will not ever practice the claimed method." *Id.* Takeda's proposed amendments provide additional allegations that prescribers and patients have directly infringed the DDI Patents using Mitigare.

As an initial matter, the Court took issue with Takeda's allegations in the First Amended Complaint that infringement of the DDI Patents "will" occur, stating that "Takeda's amended complaint offers no factual allegations that infringement, either direct or indirect has actually occurred, despite the marketing of Mitigare™ for at least ten months." D.I. 121 at 18. The use of the term "will" was a carry-over from Takeda's original Complaint, which was directed to the *prospective* infringement that would occur if Mitigare launched. Now, with Mitigare having been on the market for over a year, Takeda has amended its allegations to clarify that infringement has occurred and is continuing to occur.

Takeda also has added factual allegations which demonstrate the plausibility of its allegations of past and future infringement. The Proposed Second Amended Complaint alleges specific facts showing that Mitigare is being prescribed to patients who also are taking one of the drugs covered by the DDI Patents. Specifically, a study of pharmaceutical claims data commissioned by Takeda demonstrates that between January 1, 2015, and December 31, 2015, and in a subset of patients receiving Mitigare, 0.80% (or 8) of 994 patients studied were prescribed Mitigare concomitantly with one of the DDI drugs. PSAC ¶ 85. Moreover, as Hikma's share of the colchicine market increases, the amount of concomitant usage likely will

increase, as shown by a similar study commissioned by Takeda which demonstrated concomitant product use of Colcrys® and the DDI drugs. *Id.* ¶ 88.

The Proposed Second Amended Complaint also alleges that Hikma has encouraged healthcare providers to treat these patients in an infringing manner. New Paragraph 82 alleges that the Mitigare sell sheet, discussed *supra*, specifically directs healthcare providers to the ACR Guidelines. These Guidelines, in turn, state that, where colchicine is concomitantly administered with a PGP or CYP3A4 inhibitor (such as the four drugs covered by the DDI patents), the colchicine dose should be reduced as set forth in the FDA-approved label for Colcrys®. *Id.* ¶ 82.[7] The dose reductions listed in the Colcrys® label are the very same reductions claimed in the DDI Patents. *Id.* ¶¶ 27, 82. Accordingly, by providing the sell sheet to healthcare providers, Hikma actively encourages infringement of the DDI Patents.

While proof of individual DDI prescribing practices necessarily must await discovery, at the pleading stage, it is certainly a reasonable inference that prescribers administering Mitigare to patients concomitantly taking it with one of the DDI drugs have followed the ACR Guidelines to which Hikma has directed them, and thereby infringed the DDI Patents. Moreover, the fact that infringement of the DDI Patents may be relatively rare, does not negate Takeda's having set forth a proper claim that *some* instances of infringement have occurred, and are continuing to occur. *See, e.g., Toshiba Corp. v. Imation Corp.*, 681 F.3d 1358, 1366 (Fed. Cir. 2012) (inducement claim survives summary judgment where evidence allows conclusion that "one person somewhere in the United States" performed the claimed method).

(b) The Proposed Second Amended Complaint plausibly pleads that the patented methods can be practiced using Mitigare.

[7] The Guidelines also cite to an article co-authored by the inventor of the DDI Patents, which also recites these dose reductions.

In addition to finding Takeda's allegations of direct infringement of the DDI Patents conclusory, the Court suggested that Mitigare can never be used to practice the DDI Patents, stating that "[d]irect infringement of the DDI Patents requires a 0.3 mg dose of colchicine per day; Mitigare™ is a 0.6 mg capsule that cannot be split." D.I. 121 at 18.

In fact, as Takeda has explained, one of the DDI Patents—the '722 patent—does *not* require administration of a 0.3 daily dosage of colchicine. D.I. 115 at 19. The '722 patent clearly can be practiced by administering a 0.6 mg Mitigare capsule. *See* D.I. 109 Ex. G ('722 patent) at claim 1; *see* D.I. 109, Ex. A (Colcrys® label). PSAC ¶ 86. The claim language of the other DDI Patents refers to a "daily dosage amount" of 0.3 mg. Takeda's amended complaint alleges infringement under the doctrine of equivalents. *Id.* ¶ 87. Takeda intends to establish that a Mitigare 0.6 mg capsule taken once every other day is equivalent, for purposes of the claims, to 0.3 mg taken every day.

Although the Court stated in a footnote in its opinion that "[t]he court and Federal Circuit have already dispensed with Takeda's argument that the 0.3 mg doses may be accomplished by reducing the frequency of a 0.6 mg dose, *Takeda*, 785 F.3d at 635," D.I. 121 at 18 n.12, those prior decisions were directed to a claim for *literal* infringement, not equivalents. Equivalents is a fact question, which may not properly be adjudicated on a motion to dismiss. *Karl Kiefer Mach. Co. v. U.S. Bottlers Mach. Co.*, 113 F.2d 356, 357 (7th Cir.1940) ("[I]t is impossible for [the court] to appraise the claims or determine the extent of their scope, or the range of equivalents of their elements, without knowledge of the prior art, the history of the art, [et cetera.]").

VI. CONCLUSION

For the foregoing reasons, Takeda respectfully requests modification of the judgment of dismissal entered on May 18, 2016, to permit Takeda to file the Proposed Second Amended Complaint.

Date: June 3, 2016

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CERTIFICATE OF SERVICE

I hereby certify that on June 3, 2016, I caused the foregoing to be electronically filed with the Clerk of the Court using CM/ECF which will send electronic notification of such filing to all registered participants.

Additionally, I hereby certify that true and correct copies of the foregoing were caused to be served on June 3, 2016 upon the following individuals via electronic mail:

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